Creating New Instruments and Research Techniques

Obtaining Sufficiently Thin Specimens

The need for thin specimens stems from the fact that electrons had to pass through the specimen to create an image. If an electron encounters an obstacle, it is deflected (or loses energy). The relatively low-powered electron beam employed in the microscopes available in the 1940s and 50s could penetrate only approximately 0.1 mm of biological tissue, a distance less than the thickness of a typical cell. This meant that the tissue had to be altered in some way before an image could be generated. Three strategies were pursued to produce sufficiently thin specimens: (a) make micrographs of structures that were already sufficiently thin; (b) section the specimens; or (c) induce specimens to spread thinly. All three approaches were pursued by early electron microscopists trying to image biological material.

(A) MICROGRAPHS OF THIN BIOLOGICAL MATERIALS. Many of the earliest electron microscopists restricted themselves to thin biological materials. Two groups of researchers were noteworthy for pursuing this strategy. In order to interest biologists in using the RCA electron microscope, Zworykin had secured a National Research Council postdoctoral fellowship. It was awarded to Thomas Anderson, a recent physical chemistry Ph.D. from the California Institute of Technology. During his fellowship, Anderson worked with Stuart Mudd, head of microbiology at the University of Pennsylvania, and Wendell Stanley, from the department of plant and animal pathology at the Rockefeller Institute's Princeton Laboratory. In his first research with the electron microscope, Anderson studied bacterial and viral specimens provided by Mudd and Stanley, which were sufficiently thin for electron microscopy (Stanley & Anderson, 1941). After completing his fellowship, Anderson remained at the University of Pennsylvania, and in the 1940s focused much of his work on bacteriophages.

Francis O. Schmitt's group at MIT, which included Cecil Hall, Marie Jakus, and Richard Bear, also employed thin materials. In the early 1940s they were the only biologists with their own electron microscope (brought with a \$70,000 grant from the Rockefeller Foundation), which they used to

Shadow casting, whereby a heavy metal such as gold or chromium is deposited on the surface of a specimen at an oblique angle, which generates a shadow in the micrograph whose length corresponds to the height of the material on the specimen (Williams & Wyckoff, 1946), was another method sometimes employed with success to image viruses and bacteria.

At approximately the same time, Helmut Ruska, Ernst Ruska's brother, was appointed director of a laboratory for visiting scientists at Siemens and published his own micrographs of bacteriophages (Ruska, 1941).